

WO 99/11780

PCT/DE98/02621

1/10

MSSAVLVTLPLDPSSSFREDAPRPPVPGEEGETPPCQPSVGKVQSTKPMVSSNARNED 60
GLGEPEGRASPDSPLTRWTKSLHSLLDQDQAYLFRFTFLEREKCVDTLDFWFACNGFROM 120
NLKDTKTLRVAKAIYKRYIENNSVVSQOLKPKATKTYIRDGIKKQOIGSVMEDQAQTEIOA 180
VMEFNAYQVFLTSDIYLEYVRSGGENTAYMSNGGLGSLKVLCCGYLPTLNEEEEWTCADLK 240
CKLSPTVVGLSSKTLRATASVRSTETAENGFRSFKRSDPVNPHYVSGSYVFAPAT SANDS 300
ELSSDALTDSDMSMTDSSVDGVPPYRMGSKKQLQREMHRSVKANGQVSLPHFPRTTHRLPK 360
EMTPVEPAAFAAELISRLEKLELESRHSLEERLQQIREDEEKEGSEQALS SRDGAPVQ 420
HPLALLPSGSYEEDPQTI LDDHLSRVLKTGCGQSPGVGRYSRSPRSPDH-HQH-HHQCH 480
TLLSTGGKLPVAAACPLLGGKSFLTQTTKHVHHYTHHFAVPKTKEETAEATQVRCL 540
CPGGTDYYCYCKSKSHPKAPEFLPGEQFCGSRGGTLPKRNAKGTEPGLALSARDGCMSSA 600
AGGPQLPGEEDRSQDVWQWMLESERQSKSKPHSAQSIRKSYPLESARAAPGERVSRHL 660
LGASGHSRSVARAHFPTQDPAMPPLTPPNTLAQLEEA CRRLAEVSK9QKQRC CVASQORD 720
PNHSAAGQAGASPFANPSLAPEDHKEFKKLASVHALQASLVVTYFFCGEEIPYREMLKA 780
QSLTLGHFKEQLSKKGNRYRYFFKASDEFACGAVFEELWDDETVLPMTEGRILKVERID 840

005090-452360

Abb. 1

WO 99/11780

PCT/DE98/02621

2/10

CAGCCGTTTCGCAIGGATTTTCGGGGCCACCCGGAGGCCGAGGCTCCGGCTCCCAAAGG 60
 AGAGCTTTGCTGTAAAGAGAGAGGCTCACATGAGCCCTGCTGACTTAAGAGAGACCA 120
 AOC CGATTGCTGAGAGGAACTGGAAGAAGAAAAAGGAGGAGGAGGAAAAAAGCAAAAC 180
 AAAATCCAAACTCAGTGAGACGCTCTCCCTCACCATGAGTAGCGCGTGTAGTACTCT 240
 CCTTCCAGATCCCAGCAGCACTTCCGCGAGGATGCTCCGCGGCCCCCGTTCCGGGAGA 300
 AGAAGGGGAGACCCACCGTGTCAGCCTAGTGTGGGCAAGGTCCAGTCCACCAAACCTAT 360
 GCCCCTTTCTCTAATGCTAGGCGGAATGAAATGAGACTGGGGGAGCCCGAGGGGCGGGC 420
 CTCCCCCGATTCCCTTTGACCAGGTGGACCAAGTCTTTACACTCCTTGTGGGTGACCA 480
GGATGGTGATACCTCTTCCGGACTTTCTTGGAGAGGGAGAAATGTGTGGATACCTGGA 540
CTTCTGGTTTGTCTGTAATGGGTTTCAGGCAGATGAACCTGAAGGATACCAAACTTTGCG 600
AGTGGCCAAAGCAATCTATAAGAGGTACATTGAGAACAACAGCGTTGTCTCCAAGCAGCT 660
GAAGCCCGCCACCAAGACCTACATACGAGATGGCATCAAGAAGCAACAGATCGGCTCGGT 720
CATGTTTGACCAAGCACAGACCGAGATCCAGGCAGTGATGGAGGAAATGCTTACCAGGT 780
GTCTTGACTTCTGACATTTACCTGGAATATGTGAGGAGTGGGGGGGAAACACAGCTTA 840
 CATGAGTAACGGGGGACTGGGGAGCCTAAAGGTCTTATGTGGCTACCTCCCACTTGAA 900
 TGAAGAAGAGGAGTGGACGTGTGCCGACCTCAAGTGCAAACTCTCACCACCGTGGTTGG 960
 CTGTCCAGCAAACTCTTCCGGGCCACCGCGAGTGTGAGATCCACGGAACAGCTGAAAA 1020
 CGGATTCAGGTCTTCAAGAGAAGCGACCCAGTCAATCCTTATCACGTAGGTTCCGGCTA 1080
 TGTCTTTGACCAAGCCACCAAGCGCCAACGACAGCGAGTTATCCAGCGACCACTGACCGA 1140
 CGATTCCATGTCCATGACGGACAGTAGCGTAGATGGAGTCCCTCCTTACCGCATGGGGAG 1200
 TAAGAAACAGCTCCAGAGAGAGATGCATGCGAGTGTGAAGGCCAATGGCCAAGTGTCTCT 1260
 ACCTCATTTTCCGAGAACCACCGCCTGCCCAAGGAGATGACGCTGTGGAACCTGCTGC 1320
 CTTCCGCGCGCGAGCTCATCTCCAGGCTGGAGAACTGAAACTGGAGCTGGAAAGCCGCCA 1380
 TAGTCTGGAGGAGCGGCTGCAGCAGATCCGGGAGGATGAAGAAAAGGAGGGGTCTGAGCA 1440
 GGCCCTGAGCTCACGGGATGGAGCACC GGTCAGCACCCTTGGCCCTCTTACCCTCCGG 1500
 CAGCTATGAAGAGGACCCACAAACCATTTTGGACGACCACCTCTCCAGGGTCTCTAAGAC 1560
 CCCC GGCTGTCAATCCCTTGGTGTGGGTGCGCTACAGCCACGGTCCCGCTCCCTCCGACCA 1620
 CCACCACCAGCACCACCACCATCAGCAGTGTATACCTTCTTTGACTGGGGGCAAGCT 1680
 GCCCCCGTGGCTGCTTGGCCCCCTCCTTGGAGGCAAGAGCTTCTTGACCAACAGACGAC 1740
 GAAGCAGTTTACCACCACTACATCCACCACCACGCGCTCCCCAAGCAAGGAGGAGAT 1800
 CGAGGCAGAAGCCACACAGAGAGTCCGCTGCTCTGTCTGGGGGAACAGATTATATTG 1860
 CTACTCCAAATGCAAAAGCCACCCGAAGGCTCCAGAGCCCTGCTGGGGAGCAGTTTG 1920
 TGGCAGCAGAGGTGGTACCTTGCCAAAACGGAAATGCAAGGGCACCGAACCGGTCTTGC 1980
 ACTGTGCGCCAGGGATGGAGGGATGTCCAGTGACGCGGGGGGCCCCAGCTTCTGGGGA 2040
 AGAAGGAGACCGGTACAGGATGTCTGGCAGTGGATGTGGAGAGTGAAGCGCAGAGCAA 2100
 GTCCAAGCCCCATAGTGCCCAAAGCATAAGAAAGAGCTACCCATTGGAGTCTGCCGTGC 2160
 GGCCCCAGGAGAACGAGTCAGCCGGCACCATCTGTTGGGGGCCAGCGACACTCCGCTC 2220
 AGTGGCCCGGGCTACCCATTACCCAGGACCTGCAATGCTCCCTTACCCACCCAA 2280
 CACTTTGGCACAGCTAGAGGAAGCTGCGCAGGCTGCGAGAGGTGTGAAGCCCCAGAA 2340
 GCAGCGGTGCTGCGTGCCAGTCAGCAGAGGACAGGAACCACTCGGCTGCTGCTCAGGC 2400
 AGGAGCCTCACCCTTCGCCAACCCAGCCTGGCTCCAGAAGATCACAAGAGCCAAAGAA 2460
 ACTGGCAAGTGTCCAGCGCTCCAGGCCAGTGAAGTGTGCTACCTACTTTTCTGTGG 2520
 AGAAGAAATTCCATACAGGAGGATGCTGAAGGCTCAAAGCTTGACCTGGGGCCACTTCAA 2580
 GGAGCAGCTCAGCAAAAAGGGAATTAAGGTATTATTTCAGAAGGGGAGTGACGAATT 2640
 TGCCTGCGGAGCAGTTTTTGGAGGATCTGGGACGACGAGACAGTGCTCCCATGTACGA 2700
 AGGCAGGATCCTGGGCAAGTGGAGAGGATGACTGAGCCTTGGCTCTCTGGCGTGCAA 2760
 CCTGGGCAAGCACCTCGCGTGCACCATGGAGCCGAAGCCAGAGACCTGTCTCAGGCC 2820
 TACGC 2825

Abb. 2

WO 99/11780

PCT/DE98/02621

3/10

215 ATG AGT AGC GCC GTG TTA GTG ACT
 1 M S S A V L V T
 CTC CTT CCA GAT CCC AGC AGC AGC TTC
 L L P D P S S S F
 CGC GAG GAT GCT CCG CGG CCC CCG GTT
 R E D A P R P P V
 CCG GGA GAA GAA GGG GAG ACC CCA CCG
 P G E E G E T P P
 TGT CAG CCT AGT GTG GGC AAG GTC CAG
 C Q P S V G K V Q
 TCC ACC AAA CCT ATG CCC GTT TCC TCT
 S T K P M P V S S
 AAT GCT AGG CGG AAT GAA GAT GGA CTG
 N A R R N E D G L
 GGG GAG CCC GAG GGG CGG GCC TCC CCC
 G E P E G R A S P
 GAT TCC CCT TTG ACC AGG TGG ACC AAG
 D S P L T R W T K
 TCT TTA CAC TCC TTG TTG GGT GAC CAG
S L H S L L G D Q
 GAT GGT GCA TAC CTC TTC CGG ACT TTC
D G A Y L F R T F
 CTG GAG AGG GAG AAA TGT GTG GAT ACG
L E R E K C V D T
 CTG GAC TTC TGG TTT GCT TGT AAT GGG
L D F W F A C N G

Abb. 3

WO 99/11780

PCT/DE98/02621

4/10

TTC AGG CAG ATG AAC CTG AAG GAT ACC
F R O M N L K D T

AAA ACT TTG CGA GTG GCC AAA GCA ATC
K T L R V A K A I

TAT AAG AGG TAC ATT GAG AAC AAC AGC
Y K R Y I E N N S

GTT GTC TCC AAG CAG CTG AAG CCC GCC
V V S K O L K P A

ACC AAG ACC TAC ATA CGA GAT GGC ATC
T K T Y I R D G I

AAG AAG CAA CAG ATC GGC TCG GTC ATG
K K O O I G S V M

TTT GAC CAG GCA CAG ACC GAG ATC CAG
F D O A O T E I O

GCA GTG ATG GAG GAA AAT GCC TAC CAG
A V M E E N A Y O

GTG TTC TTG ACT TCT GAC ATT TAC CTG
V F L T S D I Y L

GAA TAT GTG AGG AGT GGG GGG GAA AAC
E Y V R S G G E N

ACA GCT TAC ATG AGT AAC GGG GGA CTG
T A Y M S N G G L

GGG AGC CTA AAG GTC TTA TGT GGC TAC
G S L K V L C G Y

CTC CCC ACC TTG AAT GAA GAA GAG GAG
L P T L N E E E E

Abb. 3

005090-12526560

WO 99/11780

PCT/DE98/02621

5/10

TGG	ACG	TGT	GCC	GAC	CTC	AAG	TGC	AAA
W	T	C	A	D	L	K	C	K
CTC	TCA	CCC	ACC	GTG	GTT	GGC	TTG	TCC
L	S	P	T	V	V	G	L	S
AGC	AAA	ACT	CTT	CGG	GCC	ACC	GCG	AGT
S	K	T	L	R	A	T	A	S
GTG	AGA	TCC	ACG	GAA	ACA	GCT	GAA	AAC
V	R	S	T	E	T	A	E	N
GGA	TTC	AGG	TCC	TTC	AAG	AGA	AGC	GAC
G	F	R	S	F	K	R	S	D
CCA	GTC	AAT	CCT	TAT	CAC	GTA	GGT	TCC
P	V	N	P	Y	H	V	G	S
GGC	TAT	GTC	TTT	GCA	CCA	GCC	ACC	AGC
G	Y	V	F	A	P	A	T	S
GCC	AAC	GAC	AGC	GAG	TTA	TCC	AGC	GAC
A	N	D	S	E	L	S	S	D
GCA	CTG	ACC	GAC	GAT	TCC	ATG	TCC	ATG
A	L	T	D	D	S	M	S	M
ACG	GAC	AGT	AGC	GTA	GAT	GGA	GTC	CCT
T	D	S	S	V	D	G	V	P
CCT	TAC	CGC	ATG	GGG	AGT	AAG	AAA	CAG
P	Y	R	M	G	S	K	K	Q
CTC	CAG	AGA	GAG	ATG	CAT	CGC	AGT	GTG
L	Q	R	E	M	H	R	S	V
AAG	GCC	AAT	GGC	CAA	GTG	TCT	CTA	CCT
K	A	N	G	Q	V	S	L	P
CAT	TTT	CCG	AGA	ACC	CAC	CGC	CTG	CCC
H	F	P	R	T	H	R	L	P

Abb. 3

ERSATZBLATT (REGEL 26)

009090-14546560

WO 99/11780

PCT/DE98/02621

6/10

AAG GAG ATG ACG CCT GTG GAA CCT GCT
 K E M T P V E P A

GCC TTC GCC GCC GAG CTC ATC TCC AGG
 A F A A E L I S R

CTG GAG AAA CTG AAA CTG GAG CTG GAA
 L E K L K L E L E

AGC CGC CAT AGT CTG GAG GAG CGG CTG
 S R H S L E E R L

CAG CAG ATC CGG GAG GAT GAA GAA AAG
 Q Q I R E D E E K

GAG GGG TCT GAG CAG GCC CTG AGC TCA
 E G S E O A L S S

CGG GAT GGA GCA CCG GTC CAG CAC CCC
 R D G A P V Q H P

CTG GCC CTC CTA CCC TCC GGC AGC TAT
 L A L L P S G S Y

GAA GAG GAC CCA CAA ACC ATT TTG GAC
 E E D P Q T I L D

GAC CAC CTC TCC AGG GTC CTC AAG ACC
 D H L S R V L K T

CCC GGC TGT CAA TCC CCT GGT GTG GGT
 P G C O S P G V G

CGC TAC AGC CCA CGG TCC CGC TCC CCC
 R Y S P R S R S P

GAC CAC CAC CAC CAG CAC CAC CAC CAT
 D H H H Q H H H H

Abb. 3

ERSATZBLATT (REGEL 26)

003090-126550

WO 99/11780

PCT/DE98/02621

7/10

CAG	CAG	TGT	CAT	ACC	CTT	CTT	TCG	ACT
Q	Q	C	H	T	L	L	S	T
GGG	GGC	AAG	CTG	CCC	CCC	GTG	GCT	GCT
G	G	K	L	P	P	V	A	A
TGC	CCC	CTC	CTT	GGA	GGC	AAG	AGC	TTC
C	P	L	L	G	G	K	S	F
CTG	ACC	AAA	CAG	ACG	ACG	AAG	CAC	GTT
L	T	K	Q	T	T	K	H	V
CAC	CAC	CAC	TAC	ATC	CAC	CAC	CAC	GCC
H	H	H	Y	I	H	H	H	A
GTC	CCC	AAG	ACC	AAG	GAG	GAG	ATC	GAG
V	P	K	T	K	E	E	I	E
GCA	GAA	GCC	ACA	CAG	AGA	GTC	CGC	TGC
A	E	A	T	Q	R	V	R	C
CTC	TGT	CCT	GGG	GGA	ACA	GAT	TAT	TAT
L	C	P	G	G	T	D	Y	Y
TGC	TAC	TCC	AAA	TGC	AAA	AGC	CAC	CCG
C	Y	S	K	C	K	S	H	P
AAG	GCT	CCA	GAG	CCC	CTG	CCT	GGG	GAG
K	A	P	E	P	L	P	G	E
CAG	TTT	TGT	GGC	AGC	AGA	GGT	GGT	ACC
Q	F	C	G	S	R	G	G	T
TTG	CCA	AAA	CGG	AAT	GCA	AAG	GGC	ACC
L	P	K	R	N	A	K	G	T
GAA	CCG	GGT	CTT	GCA	CTG	TCG	GCC	AGG
E	P	G	L	A	L	S	A	R
GAT	GGA	GGG	ATG	TCC	AGT	GCA	GCG	GGG
D	G	G	M	S	S	A	A	G

Abb. 3

ERSATZBLATT (REGEL 26)

005090-12526500

WO 99/11780

PCT/DE98/02621

8/10

GGC	CCC	CAG	CTT	CCT	GGG	GAA	GAA	GGA
G	P	Q	L	P	G	E	E	G
GAC	CGG	TCA	CAG	GAT	GTC	TGG	CAG	TGG
D	R	S	Q	D	V	W	Q	W
ATG	TTG	GAG	AGT	GAG	CGG	CAG	AGC	AAG
M	L	E	S	E	R	Q	S	K
TCC	AAG	CCC	CAT	AGT	GCC	CAA	AGC	ATA
S	K	P	H	S	A	Q	S	I
AGA	AAG	AGC	TAC	CCA	TTG	GAG	TCT	GCC
R	K	S	Y	P	L	E	S	A
CGT	GCG	GCC	CCA	GGA	GAA	CGA	GTC	AGC
R	A	A	P	G	E	R	V	S
CGG	CAC	CAT	CTG	TTG	GGG	GCC	AGC	GGA
R	H	H	L	L	G	A	S	G
CAC	TCC	CGC	TCA	GTG	GCC	CGG	GCT	CAC
H	S	R	S	V	A	R	A	H
CCA	TTT	ACC	CAG	GAC	CCT	GCA	ATG	CCT
P	F	T	Q	D	P	A	M	P
CCC	CTT	ACC	CCA	CCC	AAC	ACT	TTG	GCA
P	L	T	P	P	N	T	L	A
CAG	CTA	GAG	GAA	GCC	TGC	CGC	AGG	CTG
Q	L	E	E	A	C	R	R	L
GCA	GAG	GTG	TCG	AAG	CCC	CAG	AAG	CAG
A	E	V	S	K	P	Q	K	Q
CGG	TGC	TGC	GTG	GCC	AGT	CAG	CAG	AGG
R	C	C	V	A	S	Q	Q	R

Abb. 3

WO 99/11780

PCT/DE98/02621

9/10

GAC	AGG	AAC	CAC	TCG	GCT	GCT	GGT	CAG
D	R	N	H	S	A	A	G	Q
GCA	GGA	GCC	TCA	CCC	TTC	GCC	AAC	CCA
A	G	A	S	P	F	A	N	P
AGC	CTG	GCT	CCA	GAA	GAT	CAC	AAA	GAG
S	L	A	P	E	D	H	K	E
CCA	AAG	AAA	CTG	GCA	AGT	GTC	CAC	GCG
P	K	K	L	A	S	V	H	A
CTC	CAG	GCC	AGT	GAG	CTG	GTT	GTC	ACC
L	Q	A	S	E	L	V	V	T
TAC	TTT	TTC	TGT	GGA	GAA	GAA	ATT	CCA
Y	F	F	C	G	E	E	I	P
TAC	AGG	AGG	ATG	CTG	AAG	GCT	CAA	AGC
Y	R	R	M	L	K	A	Q	S
TTG	ACC	CTG	GGC	CAC	TTC	AAG	GAG	CAG
L	T	L	G	H	F	K	E	Q
CTC	AGC	AAA	AAG	GGA	AAT	TAC	AGG	TAT
L	S	K	K	G	N	Y	R	Y
TAT	TTC	AAG	AAG	GCG	AGT	GAC	GAA	TTT
Y	F	K	K	A	S	D	E	F
GCC	TGC	GGA	GCA	GTT	TTT	GAG	GAG	ATC
A	C	G	A	V	F	E	E	I
TGG	GAC	GAC	GAG	ACA	GTG	CTC	CCC	ATG
W	D	D	E	T	V	L	P	M
TAC	GAA	GGC	AGG	ATC	CTG	GGC	AAA	GTG
Y	E	G	R	I	L	G	K	V
GAG	AGG	ATC	GAC	TGA	2737			
E	R	I	D	Stop				

Abb. 3

005090-1426560

WO 99/11780

PCT/DE98/02621

10/10

Conductin Konstrukte	Interaktion mit				Abbau von β -Catenin in SW480 Zellen
	β -Catenin	APC #1	APC #2	GSK3 β	
	220	6	9	18	ja
	490	0	0	n.d.	ja
	1060	0	0	670	nein
	0	190	260	0	nein
	0	110	250	84	nein
	0	390	390	0	nein

Abb. 4